

Conference Paper

Blood Glucose Tendency in Alloxan-Induced Rats after Intervention with Mangosteen Peel, Clove, and Cinnamon Extracts as an Antidiabetic Response

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ABSTRACT

Diabetes mellitus continues to be a significant global health issue requiring effective treatments with minimal adverse effects. One alternative strategy is to incorporate antioxidant-rich plants into functional foods. Mangosteen peel (*Garcinia mangostana*) contains xanthenes, clove (*Syzygium aromaticum*) contains eugenol, and cinnamon (*Cinnamomum verum*) provides cinnamaldehyde and proanthocyanidin, all of which demonstrate antidiabetic properties by lowering blood glucose levels and safeguarding organs. This research aimed to assess blood glucose patterns in alloxan-induced white rats (*Rattus norvegicus*) following administration of a mixture of extracts from mangosteen peel, clove, and cinnamon. A completely randomized design with a single-factor dosage of the combined extracts was employed, with five treatment levels and three replications, yielding 15 experimental units. Blood glucose was measured using a glucometer on day 0 (pre- and post-alloxan induction), day 8, and day 15 during a 15-day treatment period. Repeated Measures ANOVA revealed a significant effect ($p < 0.05$), with a downward trend in glucose levels. The negative control group (0.5% CMC-Na) stayed around 200 mg/dL, while the positive control (metformin 9 mg/200 g BW) decreased to approximately 150 mg/dL. Groups receiving extract blends showed further reductions to 120–140 mg/dL. The most notable effect was observed with the combined extract, which lowered glucose levels to near-normal levels and maintained stability throughout the treatment period. In summary, the combined extracts from mangosteen peel, clove, and cinnamon demonstrate potential as herbal anti-diabetic agents. Further research is necessary to establish optimal dosing and assess long-term safety.

Keywords: Antioxidant, herbal therapy, mangosteen extract, mellitus diabetes

Introduction

Diabetes mellitus is a long-term metabolic disorder marked by extremely high blood sugar levels caused by impaired insulin production or action. In Indonesia, the estimated prevalence of diabetes mellitus will reach 11.3% of adults by 2024, totaling around 20.4 million cases. This reflects a rising trend in diabetes cases compared to previous years, ranking Indonesia as the fifth-highest globally. Without effective management and prevention, the number of diabetes patients in Indonesia may climb to 28.6 million by 2045 (IDF, 2024).

Although commonly used, current antidiabetic drugs are not suitable for everyone because of side effects, adverse reactions, or cost issues. There is a growing public demand for safer, more affordable, and accessible alternative and complementary medicines, particularly in Indonesia, where the

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prevalence of diabetes is very high. A key challenge is to develop new approaches that can efficiently lower blood sugar without inducing unwanted side effects.

The prevalence of diabetes mellitus is rising, along with complications that worsen patients' conditions. As a result, new prevention methods and medications are necessary to supplement or replace current treatments. Natural extracts from local ingredients, especially those traditionally used in local medicine, show significant promise and are appropriate for use in Indonesia. Further studies are required to confirm the efficacy of these alternative therapies and to promote their wider adoption in the management of diabetes.

A safer and more effective approach to managing diabetes involves using natural herbal ingredients like mangosteen rind extract (*Garcinia mangostana*), cinnamon (*Cinnamomum verum*), and cloves (*Syzygium aromaticum*). Mangosteen peel contains xanthenes with anti-inflammatory and antidiabetic effects that can help reduce oxidative stress, damaging pancreatic β -cells (John et al., 2022). Cinnamon contains active compounds, such as polyphenols, that have been shown to lower blood glucose and boost insulin sensitivity. Cloves contain eugenol, which also exhibits antidiabetic activity by lowering blood glucose levels and protecting organs (Gengatharan & Rahim, 2023; Mollazadeh & Hosseinzadeh, 2016). These natural ingredients offer a safe, affordable, and effective option for communities to decrease the incidence and complications of diabetes.

Experimental studies using alloxan-induced mice as a diabetes model are common for testing antidiabetic agents. In these studies, mangosteen (*Garcinia mangostana*) rind extract has been shown to lower blood glucose levels significantly and may help repair pancreatic β -cell damage (Darmawansyih, 2015; Maliangkay et al., 2018). Cinnamon (*Cinnamomum burmannii*) has also been shown to reduce blood sugar in animals, such as mice, due to active compounds such as cinnamaldehyde and proanthocyanidins, which exhibit hypoglycemic and antioxidant properties (Enikmawati et al., 2022; Widiyanti R & Nur, 2020). Additionally, cloves contain bioactive compounds that could enhance antidiabetic effects synergistically when combined with other ingredients (Pratiwi et al., 2024).

Using extracts from these three ingredients together is thought to enhance antidiabetic effects by lowering blood glucose and protecting pancreatic tissue, which is often damaged in diabetes mellitus. As such, studying the impact of a mixture of mangosteen peel, clove, and cinnamon extracts on alloxan-induced blood glucose in mice is a strategic step toward developing safe, natural alternative therapies. Currently, research on the effects of this specific combination on glucose levels in alloxan-induced mice is limited. These findings reflect recent advances in natural ingredient applications for diabetes treatment, highlighting this extract combination as a promising candidate for an antidiabetic agent (Enikmawati et al., 2022; Darmawansyih, 2015; Maliangkay et al., 2018; Pratiwi et al., 2024; Widiyanti & Nur, 2020). This research significantly contributes to developing alternative natural treatments for diabetes, aiming to minimize the side effects associated with synthetic drugs and offering a safer, more cost-effective option. Additionally, these findings lay the groundwork for future studies focused on identifying natural antidiabetic compounds with more targeted mechanisms of action.

This study aimed to analyze blood glucose level trends in alloxan-induced rats after administration of mangosteen peel extract, cloves, and cinnamon. It also sought to determine how effective the combination of these extracts is in lowering blood glucose levels as an antidiabetic measure.

Material and Methods

Type of research

This study is a true experiment employing a pre- and post-test control-group design. It builds on Pratiwi's previous research (2024), which involved creating a mixed tea from mangosteen peel, cinnamon, and clove. In this study, the focus is on using the optimal formula ratio (67.0:16.5:16.5 % w/w) to evaluate the antidiabetic effects—such as insulin, glucose, and lipid levels—in alloxan-induced rats.

Data collection method

The research uses a Completely Randomized Design (CRD) with a non-factorial pattern. It examines a single factor—the dose of the mixed tea extract—at five levels, with three replicates for each level. The total sample size is therefore $1 \times 5 \times 3 = 15$ samples.

Data analysis

This study examines the effect of the dose of a mixed tea extract containing mangosteen peel, cinnamon, and clove as the independent variable. The dependent variable is the antidiabetic response, assessed through blood glucose levels. Data analysis will involve a Repeated Measures ANOVA to evaluate how the antidiabetic response varies over time and with different dosage levels.

Results and Discussion

Garcinia mangostana L., known as mangosteen, is increasingly cultivated as an herbal remedy because of its medicinal benefits. It grows well in tropical areas with humid climates and consistent temperatures year-round. The fruit's skin, especially the rind, has been extensively studied for its bioactive compounds, which offer significant health benefits. Mangosteen peel contains xanthenes with anti-inflammatory and antidiabetic effects, which can help reduce oxidative stress that damages pancreatic β -cells (Chatatikun et al., 2024). Diabetes mellitus, characterized by high blood glucose, results from pancreatic β -cell dysfunction. The antioxidants in mangosteen may also protect these cells from free radical damage, enhance immune function, and lower blood glucose levels in people with diabetes (Pratiwi et al., 2024).

Cinnamomum burmannii is a sweet spice obtained from the inner bark of trees. Cinnamon is often used in herbal medicine due to its distinctive sweet scent. Traditionally, it has been employed to address digestive issues and enhance heart health, and it possesses anti-inflammatory, antimicrobial, and antioxidant properties (Geograf.id, 2023). With an IC₅₀ value of 3.24 ppm—indicating that its antioxidant content, especially the IC₅₀ value, is under 50 ppm—cinnamon exhibits a powerful antioxidant capacity (Dewita et al., 2023).

Clove (*Syzygium aromaticum*) is a spice rich in antioxidants, primarily eugenol, which plays a crucial role in shielding the body from oxidative stress and degenerative diseases. Its antioxidants combat inflammation, safeguard cells from harm, and exhibit antibacterial properties (Pramono, 2020).

Glucose levels

There were differences among initial fasting blood sugar levels, fasting blood sugar levels after alloxan administration followed by control treatment with 0.5% CMC-Na and metformin, and fasting blood sugar levels with mangosteen peel extract on days 8 and 15. The lowest fasting blood glucose levels were observed in the group with initial fasting blood glucose levels, indicating that the blood glucose levels of the experimental animals remained normal because they were not treated.

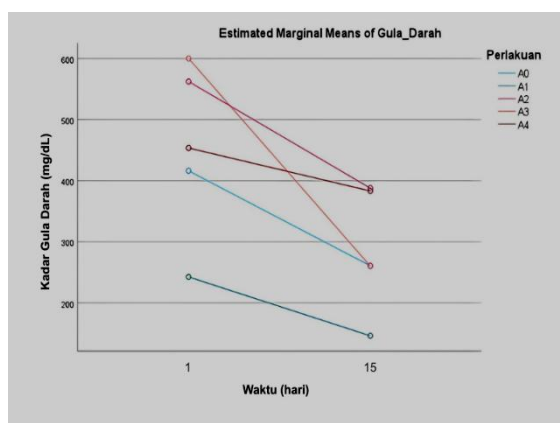


Figure 1. Graph of Blood Glucose Examination in Five Treatment Groups

The difference in fasting blood glucose levels in experimental animals before and after administering alloxan at 80 mg/kg body weight is noteworthy. Alloxan exerts two main pathological effects: it specifically inhibits glucose-triggered insulin secretion and induces insulin dependence, leading to targeted necrosis of beta cells (Wanjari et al., 2016). In a study by Sheriff et al. (2020) an alloxan dose of 150 mg/kg, prepared at 20 mg/ml and administered after a 36-hour fast, produced optimal

conditions and the lowest mortality in mice. Fasting blood sugar levels after alloxan administration, followed by mangosteen peel tea extract induction, showed a significant decrease, indicating a measurable effect ($p < 0.05$). Subsequent measurements were taken after induction with the tea extract.

The 0.5% CMC-Na control group maintained blood sugar levels around ± 600 mg/dL, confirming that alloxan effectively induced diabetes in the experimental animals. Since CMC-Na is neutral, its administration did not cause a significant decrease in blood sugar, as it is considered inert by the body after the initial rise in fasting blood glucose. Therefore, CMC-Na in this study was not effective in producing antidiabetic effects.

Following treatment A0, the positive control A1 was given metformin at 9 mg per 200g of body weight. Metformin administration resulted in notable changes in fasting blood glucose levels in the test animals, with a significant reduction of about 250 mg/dL. This aligns with the findings of Al Za'abi et al., (2021), who reported that fasting blood sugar levels decreased significantly in diabetic rats treated with either metformin alone or in combination with adenine. In contrast, the control treatment did not produce a significant change.

Fasting blood sugar levels after administering a combination of mangosteen peel extract on days 8 and 15 showed a continued significant decrease compared to levels after alloxan treatment. The most substantial reduction was in the A3 group, where blood glucose dropped from 600 mg/dL on day 1 to 280 mg/dL by day 15. This suggests that the combination of mangosteen peel extracts effectively lowers blood sugar. Conversely, the A4 group experienced the smallest decrease, with blood glucose levels changing from 450 mg/dL on day 1 to 390 mg/dL on day 15.

Mangosteen peel extract's polyphenols can lessen oxidative stress, enabling beta cells to secrete insulin. This process facilitates glucose utilization as an energy source, maintaining normal blood sugar levels (Herdiani et al., 2024). Besides the compounds in mangosteen peel, Hasmar et al (2020) noted that the decline in blood glucose was not solely due to flavonoids from clove flower extract but also involved other substances with antidiabetic effects. Cinnamaldehyde in cinnamon helps lower blood sugar by enhancing insulin sensitivity, improving pancreatic function, and inhibiting enzymes that break down carbohydrates into glucose (Analianasari et al., 2022). The most notable results were observed with a combination of extracts, which reduced glucose levels to near-normal and sustained this stability throughout the treatment period.

Conclusion

The average fasting blood glucose levels in each test animal group—including the negative control (CMC-Na 0.5%)—remained around ± 600 mg/dL after induction with mangosteen peel, cinnamon, and clove extracts. The positive control group treated with metformin (9 mg/200 g/BW) showed a reduction to approximately 250 mg/dL. The treatment groups receiving mangosteen peel, clove, and cinnamon extracts demonstrated a notable decrease, with the A3 group showing the greatest reduction. On the first day, blood glucose was 600 mg/dL, decreasing to 280 mg/dL by day 15. Conversely, the A4 group exhibited the most minor decrease, starting at 450 mg/dL and ending at 390 mg/dL on day 15. Overall, combining these herbal extracts, especially mangosteen peel, demonstrated significant antidiabetic potential, reducing fasting blood glucose to near-normal levels and maintaining stability throughout treatment. Further studies on optimal dosage and long-term safety are highly recommended.

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